MSU 4.1-406
11/22/00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#24
D.G.
12/8/00

Applicant: Alberto L. Mendoza

Serial No.: 09/082,112 Group Art Unit: 1647

Filed : 1998 May 20

For : METHOD AND VACCINE FOR TREATMENT OF PYTHIOSIS INSIDIOSI IN HUMANS AND LOWER ANIMALS

Examiner : S. Turner

Assistant Commissioner For Patents

Washington, D.C. 20231

SUPPLEMENTAL DECLARATION UNDER 37 CFR 1.132

Dear Sir:

The inventor, Alberto L. Mendoza, states as follows:

(1) Although the Examiner is correct that all proteins are produced in the endoplasmic reticulum (ER) and that at one point all proteins are intracellular, the conclusion of intracellular and extracellular proteins derived from this concept, however, has two main problems:

(a) the proteins produced by all cells at one point are intracellular; however, their activity is not fully developed until they pass through the ER where

they will acquire secondary and tertiary structures, glycosylation sites as well as leader sequences for those which will be released outside the cell (as enzymes, antibiotics, proteases, and the like); and

(b) these features are not developed at once during transit through the ER, but by small steps. This ensures to the cell that highly proteolytic or toxic proteins, which activity is required outside the cell for survival, will not damage the interior of the cell. Thus, the proteins directed by the cell outside the cytoplasm into the environment, acquire full activity only upon release. This is a very important feature of proteins outside the cell.

(2) None of the proteins in transit through the ER possess identical antigenic properties to those fully developed and released outside the cell. This is because at different points during transit through the ER the putative extracellular proteins lack secondary or tertiary structures, glycosylation sites and other immunogenic features. Therefore, when the extraction of putative extracellular proteins in transit through the ER are used as antigens they are not recognized by the immune system in the same way as those released outside the cell. This is because they lack secondary, tertiary, glycosylation sites, all features needed for the antigen presenting cells of the immune system to

mount an appropriate immune response.

(3) An extracellular antigen is defined as an immunogen (protein) that is released by the cell into the environment. This protein possesses immunogenic properties which are not encountered in those putative extracellular proteins in transit through the ER.

(4) There is no animal model which would predict any likelihood of success in humans for the vaccine used in the claimed method. Horses are not even an animal model for humans in relation to fungal diseases.

(5) ATCC 74446 and ATCC 58643 are the same organism.

(6) That the undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Alberto L. Mendoza
Date: 11/29/00